Haemodialysis

See **II / MEMBRANE SEPARATIONS / Dialysis in Medical Separations**

Kidney Dialysis

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Liquid Membranes

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Introduction

The separation of solutes by means of liquid membranes is based on a simple and well-established idea: two completely miscible liquid phases, separated by a third liquid, immiscible with either of them, can exchange solutes, provided there is a difference between their chemical potentials in the two phases and provided the intermediate liquid is able to transport them. In most cases the two miscible liquids, denoted hereafter as donor and acceptor phases, are aqueous solutions and the third (membrane) phase is an organic liquid. The configuration involving two organic solutions separated by an aqueous membrane is less popular.

The growing interest in the recovery and separation of solutes by means of liquid membranes may be related to the advantages of this separation method over the related separation operations – solid membranes and solvent extraction – as well as to the recent development of efficient liquid membrane techniques and contactors.

The main advantage of liquid membranes over polymer ones is the higher flux, owing to the very much higher diffusion coefficients of solutes in liquids than in solids. Moreover, some liquid membrane techniques allow a convective diffusion regime instead of a molecular one, which also increases fluxes. Another advantage of liquid membranes is the availability of a great number of substances which, when added to the liquid membrane phase, increase selectivity.

A liquid–membrane process can be regarded as a combination of extraction and a stripping process, which take place simultaneously in the same device. In solvent extraction, both the extractant amount and the distribution coefficient of the solute play essential roles for process efficiency, whereas in liquid membrane separation the selectivity is controlled by the kinetics of the transport process. In contrast to solvent extraction, in liquid membrane separation the amount of transferred solute is not proportional to the amount of the solvent used, in this case the membrane liquid. The relatively small amount of the latter permits the use of various highly efficient and selective – even expensive – carriers.

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Mechanisms of Solute Transfer

Like some of the solid–membrane separation methods, the difference between the chemical potentials of the solute in the donor and acceptor solutions controls the transport of the species. In other words, the concentration difference is the driving force.

There are various mechanisms for the selective transfer of solutes in the considered three-liquid-phase system. They can be divided into two groups: nonfacilitated and facilitated, or carrier-meditated, transfer mechanisms.

In nonfacilitated processes, the membrane phase is the solvent and carrier of the solute. In facilitated processes, the membrane phase is a neutral medium, dissolving a carrier, which reacts with some molecules or ions and selectively transfers them to the acceptor phase. The carrier reacts reversibly with the solute by binding it in the donor solution or at the interface between this solution and the membrane phase; it transports it across the bulk of the membrane, and releases it at the other interface. When the transfer of

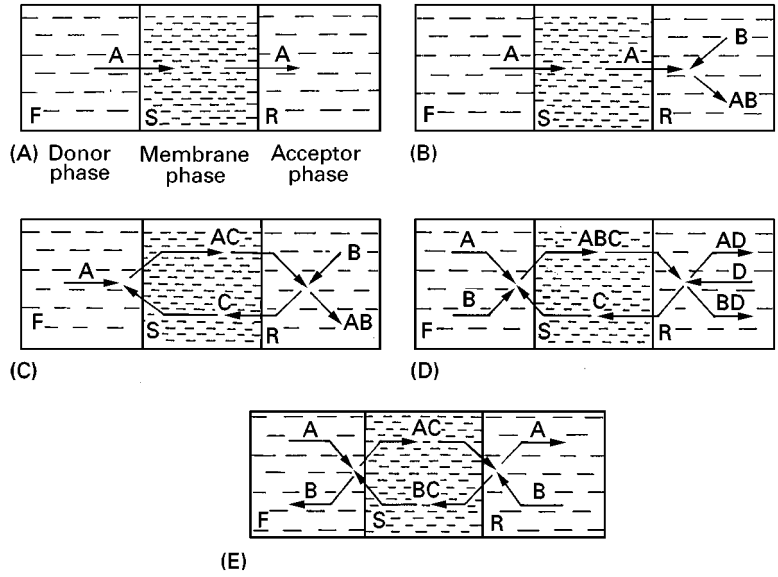

Figure 1 Basic transport mechanisms. (A) Simple nonfacilitated transport; (B) Simple uphill nonfacilitated transport; (C) facilitated uphill transport; (D) facilitated (coupled) co-transport; (E) facilitated (coupled) countertransport. See text for details.

a solute is accompanied by an equivalent transfer of one or more other solutes, it is designated as coupled transport. Depending on the direction of the accompanying transfer, the mechanisms are called co-transport and countertransport. **Figure 1** illustrates the five most popular transport mechanisms: (A) and (B) refer to nonfacilitated mechanisms, while (C)–(E) refer to facilitated mechanisms.

Nonfacilitated Mechanisms

Figure 1A shows the nonfacilitated transport of solute A from the donor solution to the membrane liquid as a result of its solubility and the low concentration in the latter. From this phase, it is transferred to the acceptor phase again for the same reasons. This process continues until the chemical potentials of the solute, i.e. its concentrations in the donor and acceptor solution, are equal. The selectivity of separation of solutes present in the donor solution mainly depends on the difference between their transfer rates, which in turn are related to their solubility in the membrane and, to a lesser extent, on the difference between their diffusion coefficients. This rather simple mechanism is of no practical interest. An example is the separation of aromatic and aliphatic hydrocarbons using water as the membrane phase.

Figure 1B shows a second example of nonfacilitated transport. The process differs from Figure 1A in that the acceptor solution has a component B which is insoluble in the membrane; it reacts irreversibly with solute A that permeates through the membrane. The reaction product AB is insoluble in the membrane and cannot diffuse back to the donor solution. In some cases an enzyme plays the role of the reagent B, transforming transported solute into products which are insoluble in the membrane. The continuous consumption of A in the acceptor solution maintains its concentration in this phase at a low level, creating a sufficient driving force to transfer the whole amount of A from the donor solution. The solute A in the form of the product AB can reach very high concentrations in the acceptor solution, which is generally of a smaller volume than the donor solution. This transfer, apparently against the concentration gradient, is known as a simple uphill transport and it has a real practical value. A typical example is the transfer of a phenol as a neutral solute which is soluble and thus permeable through the organic membrane phase. The acceptor phase is an alkaline solution that converts the phenol to an ionized salt which is not soluble or permeable through the membrane phase.

Facilitated Transport Mechanisms

In facilitated transport mechanisms the neutral membrane liquid contains an active substance C, which selectively and reversibly reacts with the permeating solute, forming a complex AC (Figure 1C). This complex is formed at the donor interface of the membrane phase and then, due to its concentration gradient, moves to the acceptor solution membrane-phase interface. The complex AC then reacts with a reagent B. As a result of this reaction, A is irreversibly bound by B, while the carrier C is restored and goes back across

the membrane to the feed–membrane interface to bind a new portion of the solute A. Because of this shuttle mechanism, small amounts of the carrier C can transfer large amounts of the solute in the acceptor phase. An example is the recovery of nitric acid from dilute solution using a small amount of the carriers tributylphosphate or trioctylphosphine oxide. The adducts formed are unstable in strongly alkaline media (the acceptor solution), where the acid is neutralized and irreversibly converted into nitrate.

In transport processes shown in Figure 1D, sometimes called facilitated co-transport, the carrier C reversibly forms an intermediate complex not only with the solute A but also with other (one or more) constituents of the donor solution. The complex ABC so formed is transported to the acceptor solution, where it reacts with another additive, D, by forming a more stable compound. The latter, like the reagent D, is insoluble in the membrane liquid. An example of this mechanism is the transport of silver which is selectively recovered from complex polymetallic nitrate solutions. The complex, transferred across the membrane, is formed by a silver cation, a nitrate anion and two molecules of the extractant triisobutylphosphine sulfide, selective for silver. In the acceptor solution, the complex is destroyed by ammonia. The chemical reaction in the acceptor phase yields ammonium nitrate, the stable silver–ammonia complex and the regenerated carrier.

Figure 1E illustrates the third, probably most often used, facilitated transport mechanism, sometimes called facilitated countertransport. In this case, ions, initially present in the donor solution, are substituted by other ions of the same type, present in a sufficient amount in the acceptor solution. This is actually an ion exchange process in which the ion-exchanging agent, the carrier C, transports in one direction one type of ion and in the opposite an equivalent amount of substituent. A typical example for this transfer is the recovery of some divalent metal cations, e.g. Cu^{2+}, from neutral or slightly acidic aqueous solutions by means of oleophilic chelating oximes. The latter transfers the metal ions to the strongly acidic acceptor solution and returns protons according to the scheme:

$$Me^{2+} + 2HR \Leftrightarrow MeR_2 + 2H^+$$

The equilibrium conditions at the two interfaces, controlled by the pH values of the aqueous phases, are chosen so that the metal–organic complex is the stable species at the donor–membrane interface, while free cations exist at the membrane–acceptor interface. This type of process is of great significance for hydrometallurgy and for the removal of heavy metals from industrial effluents.

These five types of transfer mechanisms do not exhaust all possible schemes for the selective recovery and separation of solutes by means of liquid membranes. Liquid membrane processes have been developed during the last few years on the basis of various transport and reaction mechanisms, including redox reactions. For example, the selective transfer of metals may result from the different solubility of their ions at various oxidation states. Of equal interest are some enzymatic reactions, both in the bulk of the

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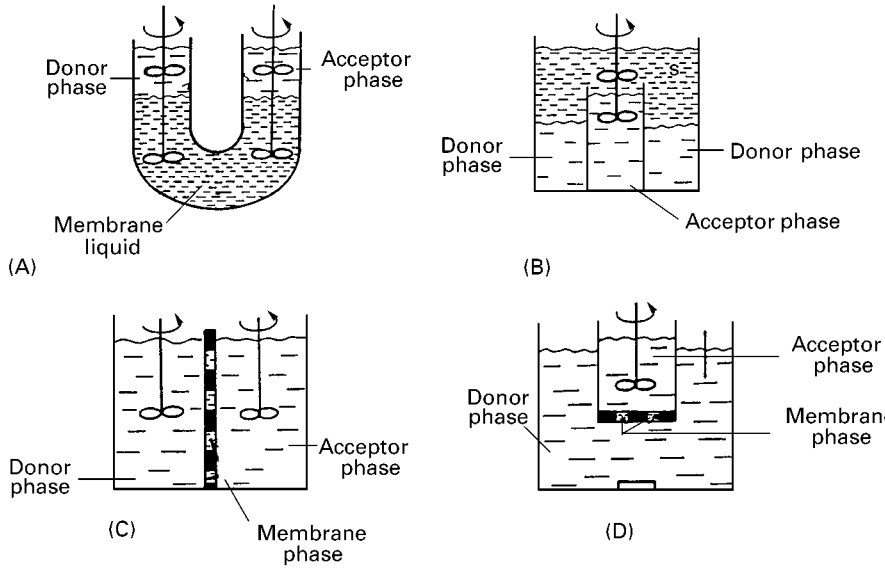

Figure 2 Bulk liquid membrane contactors for laboratory use. (A) U-tube contactor (Schulmann bridge); (B) beaker-in-beaker contactor; (C) and (D) two cells separated by supported liquid membrane.

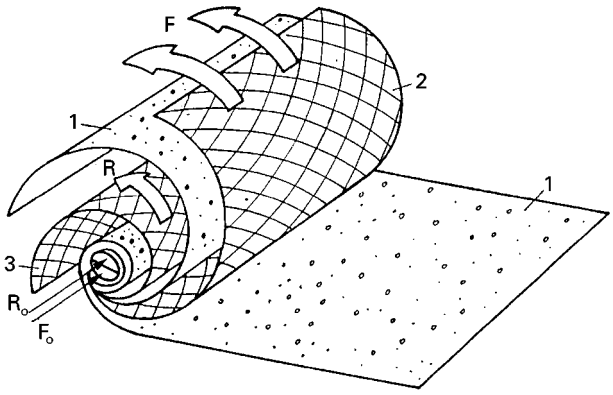

Figure 3 Spirally wound supported liquid membrane module. R, Acceptor solution; F, donor solution.

membrane and in the bulk of the acceptor solution. The reader may find further information in the Further Reading section.

Liquid Membrane Techniques

The main reason for the limited large scale application of liquid membrane processes is the lack of efficient equipment providing simultaneously large contact areas and high fluxes between the phases without deterioration of the membrane over time causing intermixing of the donor and acceptor phases. The realization of stable membranes is an extremely difficult task.

In general, liquid membrane techniques can be divided into two groups: techniques in which there is no dispersion of phases and techniques with at least one dispersed phase. The first group includes bulk liquid membranes and the supported liquid membranes, as well as some recent techniques combining elements from both techniques. The second group is mainly represented by the emulsion liquid membrane technique.

Methods Without Phase Dispersion

Simple bulk liquid membranes Several simple contact devices designed for studies of liquid–membrane processes are shown in **Figure 2**. In all, there is a common compartment for the membrane liquid. The other contactor space is divided into two compartments, one for the donor solution and the other for the acceptor solution. The interface between the membrane liquid and the other two solutions is free (A, B) or immobilized (C, D) by a solid porous membrane. The first device (A) is known as the Schulmann bridge. Devices of the type shown in Figure 1A and B are limited to laboratory experiments, but the contactors shown in Figure 2C and D find a broader application. In these devices, the membrane liquid permeates a porous membrane, which separates the donor and the acceptor solutions. In modification (D), a cylinder with an attached porous barrier rotates and stirs the donor and acceptor phases, reducing or eliminating the mass transfer resistances in these two phases. The type of device depends on whether the membrane liquid is heavier or lighter than the other two solutions.

Supported liquid membranes The laboratory contactor shown in Figure 2C is the prototype of supported liquid membrane contactors. In these devices the membrane liquid fills the pores of a 25–100 μm thick porous membrane containing pores 0.01–10 μm in diameter. The membrane is usually made of polypropylene, polysulfone or another oleophilic polymer.

Although the membrane is quite thin, the fluxes across it are very low as a result of the total immobilization of the membrane liquid in the pores, reduced free section and pore tortuosity. This is overcome by the use of large surface area modules such as the spirally wound (**Figure 3**) or containing bundles of tiny porous hollow fibres, as shown in **Figure 4**. Hollow fibre membrane modules containing fibres with diameter of 0.2–1 mm can achieve interface areas of

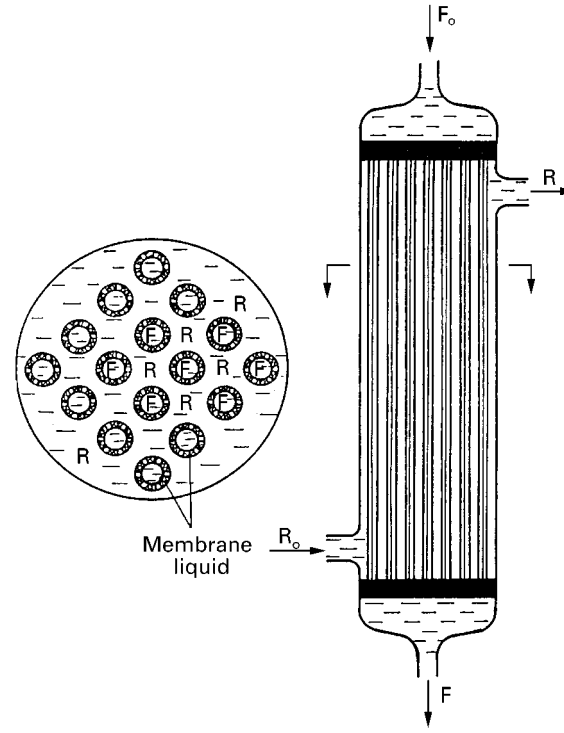

Figure 4 Hollow fibre supported liquid membrane module. R, Acceptor solution; F, donor solution; S, membrane liquid.

2000–10 000 m^2/m^3. In such modules, one of the aqueous phases flows in the lumen of the hollow fibres, while the other flows outside the fibres and the pores of the fibre walls are filled with the membrane liquid.

The insignificant amount of membrane liquid required in these modules (10 cm^3 per 1 m^2 interface), often pointed out as a major advantage, is actually the chief drawback of supported liquid membrane contactors, causing their operational instability and short life. The life of the expensive modules is shortened by the inevitable solubility of the membrane liquid in the donor and acceptor phases, by its washing out or by emulsification caused by the pressure difference on both sides of the membrane, the lateral shear force, and the change of support wettability with time. In spite of numerous design improvements, e.g. periodic or continuous reimpregnation of the membrane and partial or total gelation of the membrane liquid, this technique has not been used in industrial applications.

This instability forced researchers as early as in the 1980s to look for other solutions. The combination of this technique with stable bulk liquid membranes yielded the bulk-supported liquid membranes.

Flowing liquid membranes and contained liquid membranes In these two variants of the bulk-supported liquid membrane group, as well as in numerous subsequent modifications, the membrane liquid not only fills the pores of two closely spaced porous supports separating the donor and acceptor phase, but also the space between them, as shown in **Figures 5** and **6**. Figure 5 shows a device introduced by Teramoto *et al.*, called the flowing liquid membrane: the spirally wound module contains one additional layer and one additional porous barrier (Figure 5) in comparison with the analogous supported liquid membrane module, shown in Figure 3. Between the two, separated by porous support spacers, flows the membrane liquid, which also fills the pores of the support which are preferentially wetted by it.

In contained liquid membranes, a technique proposed by Sirkar *et al.* in the late 1980s, the donor phase flows in the lumen of a part of the capillaries, while the acceptor phase flows in the lumen of the rest of them. As Figure 6 shows, the membrane liquid filling the space outside the hollow fibres can also be set in motion. When the hollow fibre material is wetted by the membrane liquid, the pores are filled with it. In the reverse case, they are filled with the other two phases. The module shown in Figure 6, in which the inlets and the outlets of the feed and acceptor phases are located in one end of the module case, permits free elongation of the fibre package caused by the swelled membrane liquid.

The latter two membrane techniques provide significantly longer life of the contactors, as the inevitable losses of membrane fluid are compensated by the larger liquid volume. However, fluxes are lower because of higher mass transfer resistance due to the second porous support filled with immobilized liquid and the two additional diffusion boundary layers in the same phase. This drawback is, however, offset by the longer membrane life.

A further modification of the contained liquid membrane technique is the separation of the two hollow fibre packages in two modules – one where the donor liquid exchanges solutes with the membrane liquid and a second where the membrane

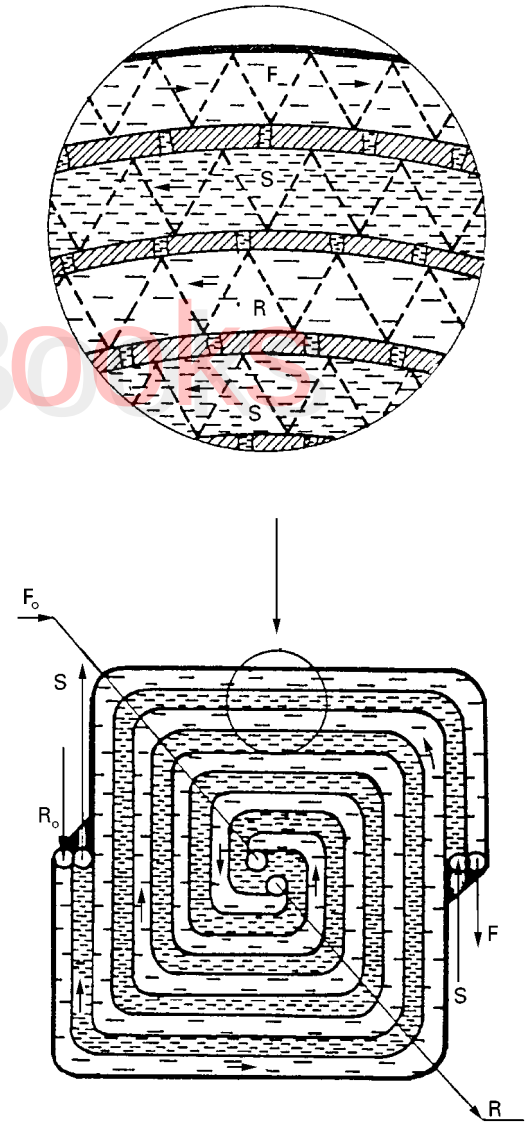

Figure 5 Spiral-type flowing liquid membrane module. R, Acceptor solution; F, donor solution; S, membrane liquid.

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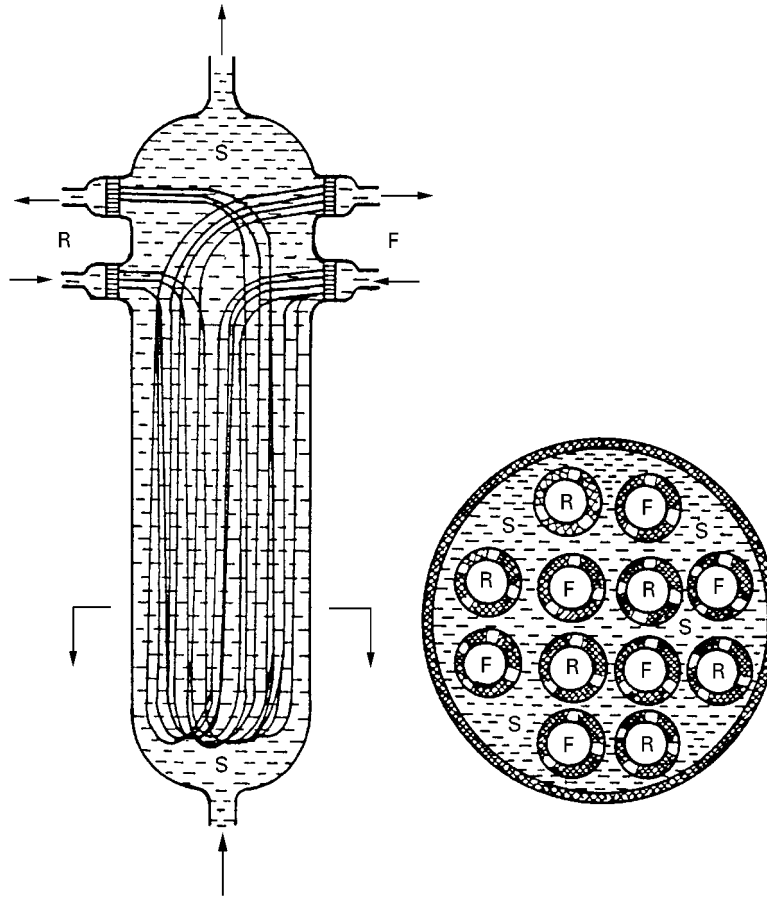

Figure 6 Contained liquid membrane contactor. R, Acceptor solution; F, donor solution; S, membrane liquid.

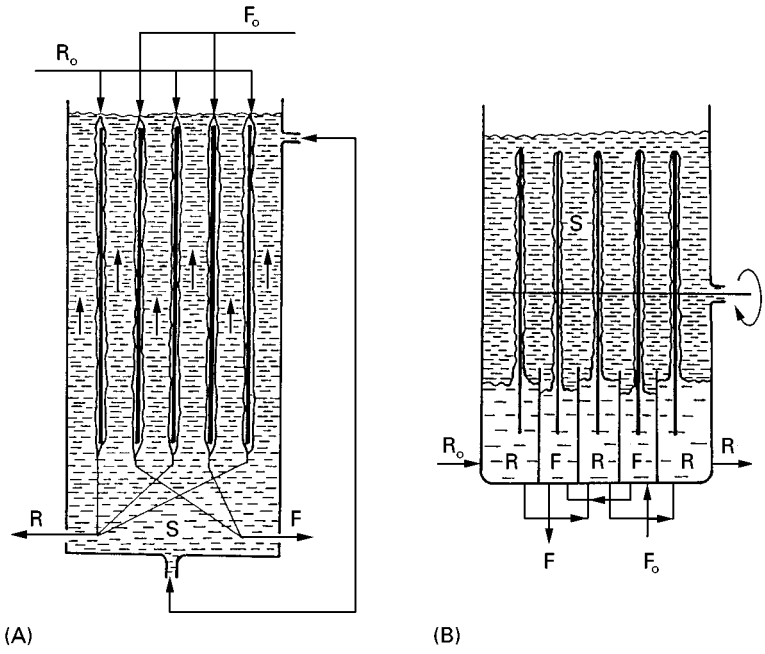

Figure 7 Liquid film pertractors: (A) falling film pertractor; (B) rotating film pertractor. R, Acceptor solution; F, donor solution; S, membrane liquid.

liquid contacts with the acceptor liquid. The membrane liquid circulates between the two devices. This technique, bearing the name two-module hollow fibre supported liquid membranes, differs little from the arrangement in a conventional extraction-stripping unit operation.

Liquid film pertraction The technique known as liquid film pertraction attempts to combine the advantages of bulk liquid membrane and supported liquid membrane. In the process all three liquids are in motion and the interfaces between the phase pairs are not immobilized, so that the transport rate in all stages of the transfer process is controlled by convective transport instead of the much slower molecular diffusion.

Two devices utilizing this technique are schematically presented in **Figure 7**. In the first one, called the falling film pertraction, shown in Figure 7A, the donor and acceptor solutions flow down the surface of alternating vertical supports. The spaces between the opposite supports, covered by films of donor and acceptor liquids, respectively, are filled with the membrane phase, flowing countercurrent to the other two. By independent control of the flow rates of the feed and acceptor phases, a significant solute accumulation in the acceptor solution can be achieved.

The second technique, rotating film pertraction uses a package of rotating horizontal discs wetted only by the feed and receptor phases. This rotation generates an intensive transfer regime in all three liquids. As Figure 7B shows, the discs, alternately mounted on a shaft, are partially immersed in the corresponding wetting solutions and on rotation form mobile films which directly contact with the membrane liquid filling the spaces between the discs.

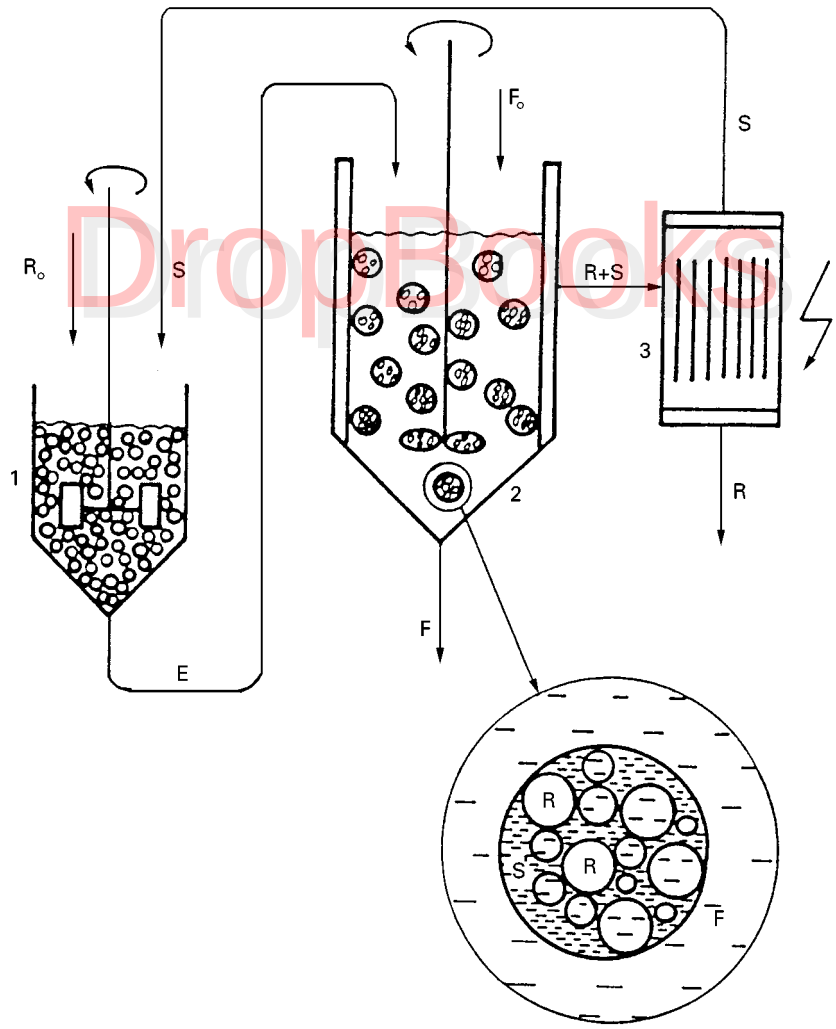

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Figure 8 Separation by emulsion liquid membranes. 1, Emulsion preparation (step 1); 2, feed treatment with the emulsion (step 2); 3, break-up of enriched emulsion (step 3). R, Acceptor solution; F, donor solution; S, membrane liquid.

The advantages of these two techniques consist in the considerably larger fluxes per unit interface and in their practically unlimited life. However, the rather low ratio between the contact interface and the bulk of the solution neutralizes, the first advantage.

Methods with Phase Dispersion

Emulsion (surfactant) liquid membranes Emulsion liquid membranes were first described in 1971 by Li in a paper dealing with the separation of aromatic and aliphatic hydrocarbons by stabilized dispersion of three liquids: the above-mentioned mixture, water and an inert hydrocarbon as a recipient phase. This technique, known as emulsion (or surfactant) liquid membranes, was the first pertraction technique developed to industrial scale.

As the name implies, the three-phase system is stabilized by an emulsifier, added to the membrane liquid, in some cases its concentration in the membrane liquid reaches 5% or more. The acceptor solution is dispersed as fine (2–20 μm) droplets in the membrane phase. The thick emulsion, stabilized by the emulsifier, is dispersed in its turn in the donor solution as globules of 1–2 mm diameter and the resulting dispersion is intensely stirred for several minutes. During this contact time, the solutes, which are more soluble in the membrane phase, are transferred from the donor phase to the intermediate phase and from there to the encapsulated acceptor solution. This transfer is very fast due to the large contact areas. After termination of the second (main) process step and dispersion settling, the enriched emulsion is separated and subjected to chemical, thermal or, most often, high voltage electrocoagulation, which breaks the emulsion into two phases. The separated membrane liquid phase is fed back for a new cycle of the process and the enriched acceptor solution phase is subjected to further treatment. The scheme in **Figure 8** illustrates this three-stage batch process which in some modifications is carried out as a continuous process. In this process, the recovery efficiency and the separation selectivity are controlled by the transfer kinetics, i.e. by the difference in the transfer rates of the individual solutes. As these rates depend on a great number of factors, for each case there is a specific optimum contact time, which can only be determined experimentally. A shorter than optimum contact time results in a lower solute recovery, while a longer contact time reduces selectivity and recovery efficiency. If the emulsion is too stable, this causes problems related to its break-up in the third process step. Irrespective of these drawbacks, the emulsion liquid membrane technique is most often investigated and practically applied.

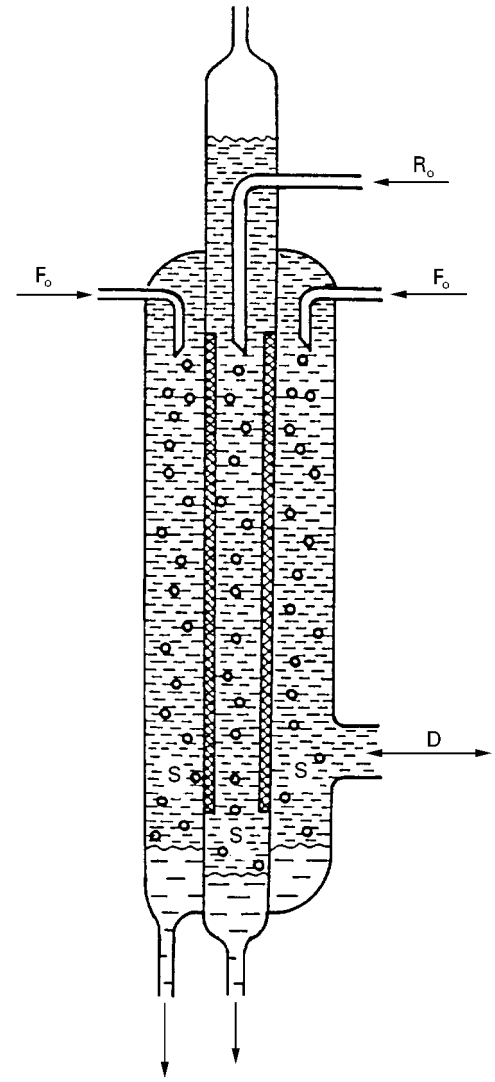

Figure 9 Two-compartment pulsating column. Applied pulsations, D, exchange the membrane liquid S between central and annular compartments across the porous wall. R, Acceptor solution; F, donor solution; S, membrane liquid.

Other techniques with phase dispersion In addition to the disadvantages listed above, the added emulsifier contaminates both the donor and acceptor phases, as in some cases its solubility in these phases exceeds that of the membrane liquid itself or of the carrier added. To avoid using surface active substances, other techniques with phase dispersion were recently proposed, two of which are illustrated in **Figures 9** and **10**.

Co-axially placed in the vertical tube is a second tube of porous hydrophobic material, e.g. porous polypropylene. As shown in Figure 9, both internal and annular spaces are filled with the membrane liquid which, under laterally applied pulsations, partially goes from one space to the other and back. The

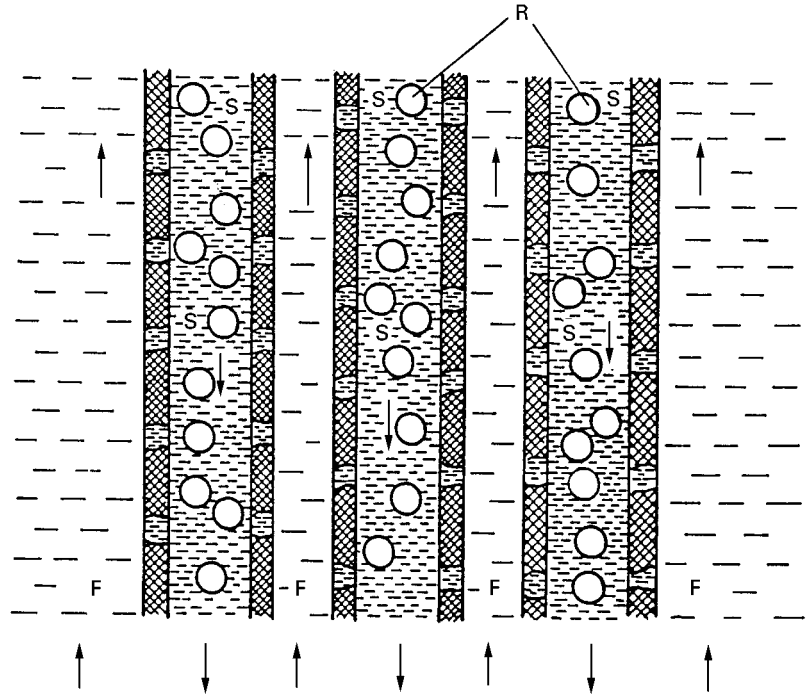

Figure 10 Combination of hollow fibre supported liquid membranes with the emulsion technique in which a nonstabilized phase R dispersed in phase S emulsion flows inside the hollow fibres.

two aqueous feed and acceptor phases are fed into the top of the central and annular space, respectively, as droplets of about 1 mm diameter. The porous filter tube does not allow intermixing of the droplets of the two aqueous phases. The aqueous droplets should be small enough to guarantee sufficient residence time of the corresponding phase in the contractor, but not too small that it penetrates into the other compartment.

The second arrangement avoiding the use of surface active substances is shown in Figure 10. The technique is a combination of hollow fibre and emulsion liquid membrane techniques without using an emulsifier for dispersion stabilization. The acceptor/membrane-phase emulsion flows in the lumen of porous capillaries wetted by the membrane liquid, filling their pores. Evidently, no intense mass transfer is possible with this technique, irrespective of the continuous wash-out of the membrane liquid by the acceptor solution dispersed in it. This drawback is, however, again compensated for by the great number of hollow fibres used and by the recirculation of the intracapillary dispersion.

Application Areas

The liquid membrane processes described above are in principle highly efficient chemical pumps selectively separating and concentrating valuable solutes. These processes have potential applications in a number of industrial areas, e.g. hydrometallurgy, electroplating and galvanic technologies, chemical and pharmaceutical industries. One of the most promising applications is in biotechnology, where pertraction, can be integrated with the basic bioprocess in order to increase process efficiency.

A very attractive feature of pertraction processes is their low investment, and in particular, their operational costs. Being a membrane operation, the separation does not involve phase transitions and therefore power consumption is very low. However, unlike solid membrane separations, the costs of lost membrane liquid and the purification of treated solutions sometimes required additionally contribute to the process costs.

The Further Reading section lists titles containing more information on various pertraction systems studied in the last 25 years.

See also: **I/Membrane Separations. II/Flotation:** Flotation Cell Design: Application of Fundamental Principles.

Further Reading

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Membrane Bioseparations

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Membrane processes are particularly well suited to the separation and purification of biological molecules since they operate at relatively low temperatures and pressures and involve no phase changes or chemical additives. Thus, these processes cause minimal denaturation, deactivation and/or degradation of highly labile biological cells or macromolecules. Although essentially all membrane processes (**Figure 1**) have been used for bioseparations, the greatest interest has been in the application of the pressure-driven processes of ultrafiltration (UF) and microfiltration (MF). Ultrafiltration membranes have pore sizes between 1 and 50 nm and are used for protein concentration, buffer exchange, desalting, clarification of antibiotics and virus clearance. There is also growing interest in the use of ultrafiltration for protein purification using high performance tangential flow filtration (HPTFF). Microfiltration membranes have a pore size between 0.05 and 10 μm and are thus used for initial clarification of protein solutions, cell harvesting and sterile filtration. In addition, ultrafiltration and microfiltration of blood are used for the treatment of a variety of metabolic and immunological disorders.

The development of membrane processes for bioseparations is very similar to the design of membrane systems for nonbiological applications. However, there are some important differences including:

1. increased concerns about deactivation or denaturation of biological molecules and cells
2. very high value (on a per unit mass basis) of most biological products (particularly recombinant therapeutic proteins)
3. tendency of biological macromolecules and cells to cause significant fouling of both ultrafiltration and microfiltration membranes
4. critical importance of validation and integrity testing in bioprocessing applications

This article provides a brief review of the historical development of membrane systems for bioseparations. This is followed by a general discussion of the

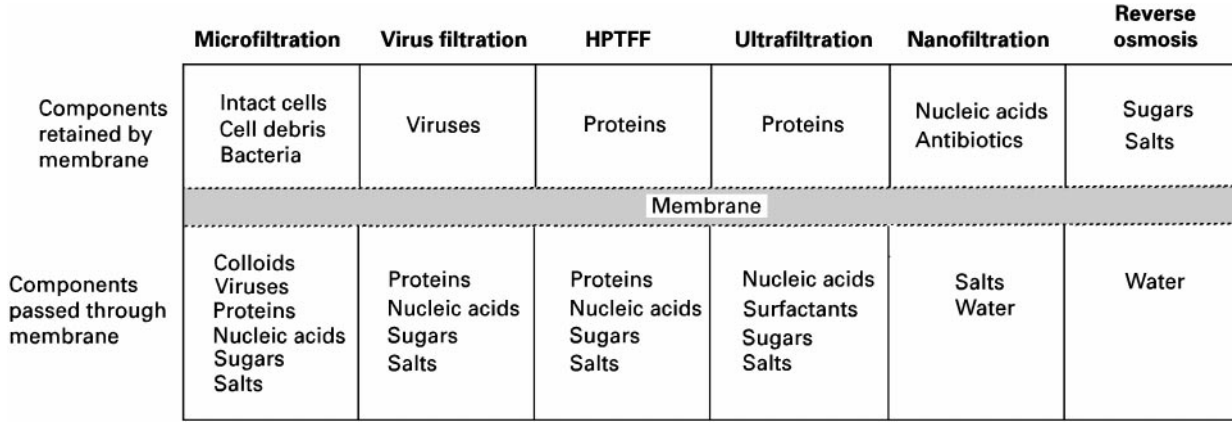

Figure 1 Classification of pressure-driven membrane processes showing typical bioprocessing applications.